L.HELMS

P#9

OIPE

RAW SEQUENCE LISTING DATE: 07/18/2001
PATENT APPLICATION: **US/09/509,098** TIME: 10:20:42

Input Set : **A:\53466274.app**
Output Set: **N:\CRF3\07182001\I509098.raw**

ρ∫

ENTERED

```
 3 <110> APPLICANT: TSUCHIYA, MASAYUKI
 5 <120> TITLE OF INVENTION: NATURAL HUMANIZED ANTIBODY
 7 <130> FILE REFERENCE: 053466/0274
 9 <140> CURRENT APPLICATION NUMBER: 09/509,098
10 <141> CURRENT FILING DATE: 2000-03-22
12 <150> PRIOR APPLICATION NUMBER: PCT/JP98/04469
13 <151> PRIOR FILING DATE: 1998-10-02
15 <150> PRIOR APPLICATION NUMBER: JP 9-271726
16 <151> PRIOR FILING DATE: 1997-10-03
18 <160> NUMBER OF SEQ ID NOS: 203
20 <170> SOFTWARE: PatentIn Ver. 2.1
22 <210> SEQ ID NO: 1
23 <211> LENGTH: 394
24 <212> TYPE: DNA
25 <213> ORGANISM: Murine sp.
27 <220> FEATURE:
28 <221> NAME/KEY: sig_peptide
29 <222> LOCATION: (1)..(72)
31 <220> FEATURE:
32 <221> NAME/KEY: mat_peptide
33 <222> LOCATION: (73)..(393)
35 <220> FEATURE:
36 <221> NAME/KEY: CDS
37 <222> LOCATION: (1)..(393)
39 <220> FEATURE:
40 <223> OTHER INFORMATION: Description of Artificial Sequence: cDNA coding
41       for L chain V region of anti-HM1.24 antibody
43 <400> SEQUENCE: 1
44 atg ggc ttc aag atg gag tca cat ttt ctg gtc ttt gta ttc gtg ttt    48
45 Met Gly Phe Lys Met Glu Ser His Phe Leu Val Phe Val Phe Val Phe
46               -20             -15             -10
48 ctc tgg ttg tct ggt gtt gac gga gac att gtg atg acc cag tct cac    96
49 Leu Trp Leu Ser Gly Val Asp Gly Asp Ile Val Met Thr Gln Ser His
50               -5          -1  1               5
52 aaa ttc atg tcc aca tca gta gga gac agg gtc agc atc acc tgc aag   144
53 Lys Phe Met Ser Thr Ser Val Gly Asp Arg Val Ser Ile Thr Cys Lys
54       10              15              20
56 gcc agt cag gat gtg aat act gct gta gcc tgg tat caa caa aaa cca   192
57 Ala Ser Gln Asp Val Asn Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro
58   25              30              35              40
60 gga caa tcg cct aaa cta ctg att tac tcg gca tcc aac cgg tac act   240
61 Gly Gln Ser Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asn Arg Tyr Thr
62               45              50              ·55
64 gga gtc cct gat cgc atc act ggc agt gga tct ggg acg gat ttc act   288
65 Gly Val Pro Asp Arg Ile Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr
66               60              65              70
68 ttc acc atc agc agt gtg cag gcg gaa gac ctg gca ctt tat tac tgt   336
```

```
69 Phe Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Leu Tyr Tyr Cys
70          75                  80                  85
72 cag caa cat tat agt act cca ttc acg ttc ggc tcg ggg aca aag ttg    384
73 Gln Gln His Tyr Ser Thr Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu
74      90                  95                  100
76 gaa ata aaa c                                                      394
77 Glu Ile Lys
78 105
81 <210> SEQ ID NO: 2
82 <211> LENGTH: 131
83 <212> TYPE: PRT
84 <213> ORGANISM: Murine sp.
86 <220> FEATURE:
87 <223> OTHER INFORMATION: Description of Artificial Sequence: Amino acid
88      sequence of L chain V region of mouse anti-HM1.24
89      antibody
91 <400> SEQUENCE: 2
92 Met Gly Phe Lys Met Glu Ser His Phe Leu Val Phe Val Phe Val Phe
93              -20                 -15                 -10
95 Leu Trp Leu Ser Gly Val Asp Gly Asp Ile Val Met Thr Gln Ser His
96          -5                  -1  1                  5
98 Lys Phe Met Ser Thr Ser Val Gly Asp Arg Val Ser Ile Thr Cys Lys
99      10                  15                  20
101 Ala Ser Gln Asp Val Asn Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro
102 25                  30                  35                  40
104 Gly Gln Ser Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asn Arg Tyr Thr
105                 45                  50                  55
107 Gly Val Pro Asp Arg Ile Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr
108                 60                  65                  70
110 Phe Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Leu Tyr Tyr Cys
111             75                  80                  85
113 Gln Gln His Tyr Ser Thr Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu
114     90                  95                  100
116 Glu Ile Lys
117 105
121 <210> SEQ ID NO: 3
122 <211> LENGTH: 418
123 <212> TYPE: DNA
124 <213> ORGANISM: Murine sp.
126 <220> FEATURE:
127 <221> NAME/KEY: sig_peptide
128 <222> LOCATION: (1)..(57)
130 <220> FEATURE:
131 <221> NAME/KEY: mat_peptide
132 <222> LOCATION: (58)..(417)
134 <220> FEATURE:
135 <221> NAME/KEY: CDS
136 <222> LOCATION: (1)..(417)
138 <220> FEATURE:
```

RAW SEQUENCE LISTING   DATE: 07/18/2001
PATENT APPLICATION: **US/09/509,098**   TIME: 10:20:42

Input Set : **A:\53466274.app**
Output Set: **N:\CRF3\07182001\I509098.raw**

```
139 <223> OTHER INFORMATION: Description of Artificial Sequence: cDNA coding
140        for H chain V region of mouse anti-HM1.24
141        antibody
143 <400> SEQUENCE: 3
144 atg gaa tgt aac tgg ata ctt cct ttt att ctg tca gta act tca ggt    48
145 Met Glu Cys Asn Trp Ile Leu Pro Phe Ile Leu Ser Val Thr Ser Gly
146                    -15              -10                  -5
148 gcc tac tca cag gtt caa ctc cag cag tct ggg gct gag ctg gca aga    96
149 Ala Tyr Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg
150             -1  1               5                  10
152 cct ggg gct tca gtg aag ttg tcc tgc aag gct tct ggc tac acc ttt   144
153 Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe
154         15                  20                  25
156 act ccc tac tgg atg cag tgg gta aaa cag agg cct gga cag ggt ctg   192
157 Thr Pro Tyr Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu
158  30                  35                  40                  45
160 gaa tgg att ggg tct att ttt cct gga gat ggt gat act agg tac agt   240
161 Glu Trp Ile Gly Ser Ile Phe Pro Gly Asp Gly Asp Thr Arg Tyr Ser
162                  50                  55                  60
164 cag aag ttc aag ggc aag gcc aca ttg act gca gat aaa tcc tcc agt   288
165 Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser
166             65                  70                  75
168 aca gcc tac atg caa ctc agc atc ttg gca ttt gag gac tct gcg gtc   336
169 Thr Ala Tyr Met Gln Leu Ser Ile Leu Ala Phe Glu Asp Ser Ala Val
170         80                  85                  90
172 tat tac tgt gca aga gga tta cga cga ggg ggg tac tac ttt gac tac   384
173 Tyr Tyr Cys Ala Arg Gly Leu Arg Arg Gly Gly Tyr Tyr Phe Asp Tyr
174      95                  100                  105
176 tgg ggc caa ggc acc act ctc aca gtc tcc tca g                     418
177 Trp Gly Gln Gly Thr Thr Leu Thr Val Ser Ser
178 110                  115                  120
181 <210> SEQ ID NO: 4
182 <211> LENGTH: 139
183 <212> TYPE: PRT
184 <213> ORGANISM: Murine sp.
186 <220> FEATURE:
187 <223> OTHER INFORMATION: Description of Artificial Sequence: Amino acid
188        sequence of H chain V region of mouse anti-
189        HM1.24 antibody
191 <400> SEQUENCE: 4
192 Met Glu Cys Asn Trp Ile Leu Pro Phe Ile Leu Ser Val Thr Ser Gly
193                    -15              -10                  -5
195 Ala Tyr Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg
196             -1  1               5                  10
198 Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe
199         15                  20                  25
201 Thr Pro Tyr Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu
202  30                  35                  40                  45
204 Glu Trp Ile Gly Ser Ile Phe Pro Gly Asp Gly Asp Thr Arg Tyr Ser
```

RAW SEQUENCE LISTING   DATE: 07/18/2001
PATENT APPLICATION: US/09/509,098   TIME: 10:20:42

Input Set : A:\53466274.app
Output Set: N:\CRF3\07182001\I509098.raw

```
205                 50                  55                  60
207 Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser
208             65                  70                  75
210 Thr Ala Tyr Met Gln Leu Ser Ile Leu Ala Phe Glu Asp Ser Ala Val
211         80                  85                  90
213 Tyr Tyr Cys Ala Arg Gly Leu Arg Arg Gly Gly Tyr Tyr Phe Asp Tyr
214     95                  100                 105
216 Trp Gly Gln Gly Thr Thr Leu Thr Val Ser Ser
217 110             115                 120
221 <210> SEQ ID NO: 5
222 <211> LENGTH: 11
223 <212> TYPE: PRT
224 <213> ORGANISM: Artificial Sequence
226 <220> FEATURE:
227 <223> OTHER INFORMATION: Description of Artificial Sequence: CDR (1) of L
228       chain V region of anti-HM1.24 antibody
230 <400> SEQUENCE: 5
231 Lys Ala Ser Gln Asp Val Asn Thr Ala Val Ala
232   1               5                   10
235 <210> SEQ ID NO: 6
236 <211> LENGTH: 7
237 <212> TYPE: PRT
238 <213> ORGANISM: Artificial Sequence
240 <220> FEATURE:
241 <223> OTHER INFORMATION: Description of Artificial Sequence: CDR (2) of L
242       chain V region of anti-HM1.24 antibody
244 <400> SEQUENCE: 6
245 Ser Ala Ser Asn Arg Tyr Thr
246   1               5
249 <210> SEQ ID NO: 7
250 <211> LENGTH: 9
251 <212> TYPE: PRT
252 <213> ORGANISM: Artificial Sequence
254 <220> FEATURE:
255 <223> OTHER INFORMATION: Description of Artificial Sequence: CDR (3) of L
256       chain V region of anti-HM1.24 antibody
258 <400> SEQUENCE: 7
259 Gln Gln His Tyr Ser Thr Pro Phe Thr
260   1               5
263 <210> SEQ ID NO: 8
264 <211> LENGTH: 5
265 <212> TYPE: PRT
266 <213> ORGANISM: Artificial Sequence
268 <220> FEATURE:
269 <223> OTHER INFORMATION: Description of Artificial Sequence: CDR (1) of H
270       chain V region of anti-HM1.24 antibody
272 <400> SEQUENCE: 8
273 Pro Tyr Trp Met Gln
274   1               5
```

Input Set : A:\53466274.app
Output Set: N:\CRF3\07182001\I509098.raw

```
277 <210> SEQ ID NO: 9
278 <211> LENGTH: 16
279 <212> TYPE: PRT
280 <213> ORGANISM: Artificial Sequence
282 <220> FEATURE:
283 <223> OTHER INFORMATION: Description of Artificial Sequence: CDR (2) of H
284       chain V region of anti-HM1.24 antibody
286 <400> SEQUENCE: 9
287 Ser Ile Phe Gly Asp Gly Asp Thr Arg Tyr Ser Gln Lys Phe Lys Gly
288   1               5                  10                  15
291 <210> SEQ ID NO: 10
292 <211> LENGTH: 11
293 <212> TYPE: PRT
294 <213> ORGANISM: Artificial Sequence
296 <220> FEATURE:
297 <223> OTHER INFORMATION: Description of Artificial Sequence: CDR (3) of H
298       chain V region of anti-HM1.24 antibody
300 <400> SEQUENCE: 10
301 Gly Leu Arg Arg Gly Gly Tyr Tyr Phe Asp Tyr
302   1               5                  10
305 <210> SEQ ID NO: 11
306 <211> LENGTH: 379
307 <212> TYPE: DNA
308 <213> ORGANISM: Artificial Sequence
310 <220> FEATURE:
311 <223> OTHER INFORMATION: Description of Artificial Sequence: DNA coding for
312       humanized L chain V region of anti-HM1.24
313       antibody
315 <220> FEATURE:
316 <221> NAME/KEY: sig_peptide
317 <222> LOCATION: (1)..(57)
319 <220> FEATURE:
320 <221> NAME/KEY: mat_peptide
321 <222> LOCATION: (58)..(378)
323 <220> FEATURE:
324 <221> NAME/KEY: CDS
325 <222> LOCATION: (1)..(378)
327 <400> SEQUENCE: 11
328 atg gga tgg agc tgt atc atc ctc tcc ttg gta gca aca gct aca ggt    48
329 Met Gly Trp Ser Cys Ile Ile Leu Ser Leu Val Ala Thr Ala Thr Gly
330               -15              -10                 -5
332 gtc cac tcc gac atc cag atg acc cag agc cca agc agc ctg agc gcc    96
333 Val His Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
334           -1  1           5                  10
336 agc gtg ggt gac aga gtg acc atc acc tgt aag gct agt cag gat gtg   144
337 Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val
338       15                  20                 25
340 aat act gct gta gcc tgg tac cag cag aag cca gga aag gct cca aag   192
341 Asn Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
```

Use of n and/or Xaa has been detected in the Sequence Listing.
Review the Sequence Listing to insure a corresponding
explanation is presented in the <220> to <223> fields of
each sequence using n or Xaa.

VERIFICATION SUMMARY DATE: 07/18/2001
PATENT APPLICATION: **US/09/509,098** TIME: 10:20:43

Input Set : **A:\53466274.app**
Output Set: **N:\CRF3\07182001\I509098.raw**

```
L:3747 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:136
L:3750 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:136
L:3753 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:136
L:4243 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:157
L:5092 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:199
L:5095 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:199
L:5098 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:199
L:5101 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:199
```